Remarks

Upon entry of the current amendments, claims 24 to 104 will be pending in this application. Claims 40, 50, 51, 64, 76, 100, 101, and 102 have been amended. Applicants expressly assert that these claims were amended for the sole purpose of facilitating prosecution or to more clearly define the invention claimed by the Applicant. Support for the amendments is found, for example, on page 96, lines 19-22 and on page 84, lines 29-31. New claims 103 and 104 have been added. Support for these new claims can be found in the specification, for example, on page 84, lines 29-31, and on page 9, lines 12-13 and lines 26-30. No new matter has been added by way of the amendments to the claims.

Applicants thank the Examiner and her supervisor for the courtesy of the Examiner interview on August 13, 2002 to discuss the following rejections.

I. Rejections under 35 U.S.C. §101

The Examiner has rejected claims 24-102 under 35 U.S.C. §101 for allegedly lacking either a specific and substantial asserted utility or a well established utility. Specifically, the Examiner states on page 3, last line, through page 4, line 18, that:

> However, the assertion that the protein and/or nucleic acid of the instant invention can be used in the diagnosis or treatment of diseases or disorders is also not a specific and substantial utility, and is based on both the tissue expression of CRCGCL and the assumption that the protein is a receptor in the cytokine receptor family, which as a family are involved in myriad of biological pathways and activities and disorders... A stated belief that a correlation exists between the polypeptides and any number of diseases is not sufficient guidance to use the claimed polypeptides to treat and/or diagnose a particular disease.

Applicants respectfully disagree and traverse.

The Examiner appears to be prejudicing the logical manner in which Applicants arrived at the assertion that CRCGCL is involved in immune disorders. However, as stated in the M.P.E.P. section 2107.02 part III:

> *Langer* and subsequent cases direct the Office to presume that a statement of utility made by an applicant is true. See *In re Langer*, 503 F.2d at 1391, 183 USPQ at 297; In re Malachowski, 530 F.2d 1402, 1404, 189 USPQ 432, 435 (CCPA 1976); *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). For obvious reasons of efficiency and in deference to an applicant's understanding of his or her invention, when a statement of utility is evaluated, Office personnel should not begin by questioning the truth of the statement of utility. Instead, any inquiry must start by asking if there is any reason to question the truth of the statement of utility. This can be done by simply evaluating the logic of the statements made, taking into

> consideration any evidence cited by the applicant. If the asserted utility is credible (i.e., believable based on the record or the nature of the invention), a rejection based on "lack of utility" is not appropriate. Clearly, Office personnel should not begin an evaluation of utility by assuming that an asserted utility is likely to be false, based on technical field of the invention or for other general reasons.

Thus, Applicants respectfully submit that the Examiner's reason for rejecting the claims is improper per the M.P.E.P. For the Examiner's convenience, a review of the facts disclosed in the specification is presented below.

Applicants assert that the claimed CRCGCL is a cytokine receptor (*see* e.g. page 1, lines 10-11 of the specification) based upon the following:

i) tissue expression in immune specific tissues such as lymph nodes and spleen (*see*, for example, page 9, line 17 and line 29 through page 10, line 2) of the specification);

ii) the fact that CRCGCL exhibits homology to the IL-2 receptor common gamma chain (*see* specification page 9, lines 9-11). IL-2 is the principle autocrine growth factor for most T cells that mediates T cell proliferation during activation (*see* Abbas, A. K. et al., Cellular and Molecular Immunology, pages 156-157, 2nd edition (1994) submitted herewith as Exhibit G);

iii) the claimed protein contains a predicted Jak Box (*see* page 9, lines 16-17 of the specification); and

iv) the clone was found in only activated T cells as opposed to resting T cells (*see* specification 10, line 23).

This last fact is further corroborated by the executed Rule 132 Declaration of Dr. Paul Moore, submitted herewith. It is well known in immunological arts that the activation of lymphocytes (which include B and T-cells) generally includes both proliferation and differentiation of lymphocytes (*see* Abbas, A. K. et al., Cellular and Molecular Immunology, pages 9-10, 2nd edition (1994), submitted herewith as Exhibit F). As evidence of the credibility of the claimed protein's utility to diagnose or treat T cell-mediated immune or autoimmune disorders (specifically, that antagonists to CRCGCL receptor protein in the form of a soluble extracellular portion (*see* page 84, lines 29-31 and page 9, lines 12-13 and 26-30) can be used to inhibit the proliferation of T-cells and, thus, those T cell mediated diseases listed on page 10 of the specification), Applicants submit herewith the Rule 132 Declaration of Dr. Paul Moore, which confirms that the expression of the claimed CRCGCL receptor

protein is limited to *activated* T-cells, as opposed to resting T-cells. Dr. Moore asserts that experiments were performed in which the CRCGCL receptor protein's mRNA expression profile in both resting (unactivated) and activated T-cells were isolated and analyzed (*see* paragraphs 6 and 7 and Exhibit A of Dr. Moore's Rule 132 Declaration). As shown in Exhibit A, the CRCGCL receptor protein is upregulated approximately 10-1000 fold in activated T-cells over resting T-cells, thereby confirming the assertion made in the specification that the claimed CRCGCL receptor protein's expression is limited to only activated T-cells (*see* page 10, line 23 in the specification). As discussed above, this expression profile is significant, as it suggests a role for this receptor in the immune response (T-cell activation), which entails both cell proliferation and differentiation. Thus, Applicants respectfully submit that the claimed protein can be used to diagnose or treat T cell-mediated immune and autoimmune disorders, such as, for example, antagonists to CRCGCL receptor can be used to inhibit T cell proliferation.

Based on the facts discussed above, Applicants respectfully submit that one of skill in the art would find it more likely than not true that the claimed CRCGCL is a cytokine receptor. In fact, the Examiner admits that the evidence provided is supportive of the CRCGCL protein being a receptor of this family (*see* Paper No. 26, page 2, section 3).

Moreover, the CRCGCL receptor of the instant invention has been *shown* through experimental evidence (i.e., the previously submitted Rule 132 Declaration of Dr. Paul Moore filed July 26, 2001, Paper No. 18) to bind a cytokine and to stimulate a Jak-STAT signal transduction pathway, as described in the specification (*see* page 147, line 12), thereby corroborating Applicant's assertions discussed above. The experimental evidence provided in the declaration further illustrates the ability of soluble, extracellular fragments of CRCGCL to bind a cytokine and inhibit the Jak-STAT pathway, confirming the therapeutic use of such CRCGCL fragments to treat immune diseases and in particular, T cell-mediated immune and autoimmune diseases by inhibiting the action of CRCGCL (*see e.g.*, specification at page 84, lines 29-30; page 113, lines 22-23; and page 117, lines 2-4). Regarding the previously submitted declaration the Examiner responds:

> However, the declaration is not a substitute for information not disclosed in the specification as filed, and is not commensurate with the scope of the claims. The specification did not envision a specific cytokine to which CRCGCL would bind, and did not teach that the cytokine TSLP would bind the receptor.

Applicants disagree and traverse.

Applicants submit that the purpose of the declaration was not to name a specific cytokine as a ligand for the CRCGCL receptor, but rather, to corroborate Applicant's assertion that CRCGCL is indeed a cytokine receptor and the predicted use of CRCGCL in immune cell regulation through cytokine binding and activation of a Jak-STAT signal transduction pathway (*see* page 2, section 3 and page 3, lines 2-3 of the Declaration). The evidence in the submitted declaration that CRCGCL binds a cytokine (TSLP) and activates the Jak-STAT signal transduction pathway, supports the assertion that CRCGCL is a cytokine receptor.

The Examiner states that not all of the biological activities of a protein need to be known to obtain a patent, but that there must be some specific and substantial activity or function known (*see* Paper No. 26, page 5, lines 12-13, emphasis added). Applicants respectfully submit that proof of a specific or substantial utility is not the proper legal standard upon which to evaluate utility. The proper standard is a reasonable correlation, not a statistical certainty, such that one of skill in the art would find it more likely than not true (M.P.E.P. 2107.03, page 2100-43, section I). The proper legal standard to judge utility does not rest upon whether data is disclosed, rather, the standard is whether one of skill in the art, upon reading the entire specification, would find the asserted utilities for the claimed invention an "inherently unbelievable undertaking or involve implausible scientific principle" (*see* In re Brana, 51 F.3d 1560, 1566 (Fed Cir. 1995)). Applicants respectfully submit that the present asserted utilities are not implausible to one of skill in the art, as will be discussed below.

In order to further support the fact that one of skill in the art would find that a specific, substantial, and credible utility was in fact asserted in the specification of the instant application, Applicants hereby submit an executed Rule 132 Declaration by Dr. Thi-Sau Migone. Dr. Migone's declaration demonstrates that she is an immunologist and is therefore considered one of skill in the cytokine arts (see paragraph 1 of Dr. Migone's Rule 132 Declaration and the accompanying Exhibit B). Further, Dr. Migone's declaration contends that after reading the specification, she understood that the CRCGCL receptor protein demonstrates homology to the IL-2 receptor gamma chain, that the CRCGCL receptor protein is only expressed in activated T-cells (see Dr. Paul A. Moore's Rule 132 Declaration submitted herewith), and that the CRCGCL receptor protein possesses a Jak box, and was found to interact with a Jak kinase (see paragraphs 5, 6, 11, 12 and 13 of Dr. Migone's Rule 132 Declaration). Dr. Migone also understood that the specification asserts that the

CRCGCL receptor protein can be used to diagnose or treat immune and autoimmune disorders, specifically, for example, that antagonists to CRCGCL receptor protein can be used to inhibit the proliferation of T-cells (see paragraphs 14, 15 and 17 of Dr. Migone's Rule 132 Declaration). This understanding was based upon the teachings of the specification as well as what was known in the field of cytokine research at the time the application was filed (see paragraphs 7, 9, 10, 16 of Dr. Migone's Rule 132 Declaration and the accompanying Exhibits C, D, and E).

Applicants have shown that CRCGCL has biological activities that are reasonably correlated with the utilities asserted in the specification, namely i) immune cell regulation through cytokine binding and activation of the Jak-STAT signal transduction pathway and ii) the treatment of deficiencies or disorders of the immune system, by activating (using the claimed protein) or inhibiting (using the claimed antagonists or extracellular soluble fragments) immune cell proliferation and differentiation. Furthermore, the asserted utilities for CRCGCL are specific (the vast majority of proteins do not bind cytokine, activate a Jak-STAT signal transduction pathway, or affect immune cell proliferation) and substantial ("the general rule [is] that the treatments of specific diseases or conditions meet the criteria of 35 U.S.C. §101." (Revised Interim Guidelines Training Manual p. 6)). In addition, as supported by the above described Rule 132 Declarations, these utilities are credible. Therefore, the only reasonable conclusion that can be reached based on the data and assertions of utility in the specification, supported by the submitted declarations, is that the present invention is useful for the purposes asserted in the specification. Because Applicants' assertions of utility are sufficient to satisfy the requirements of 35 U.S.C. § 101, it is respectfully requested that the Examiner's rejection of the claims under 35 U.S.C. § 101 be reconsidered and withdrawn.

II. Rejections under 35 U.S.C. §112, first paragraph

A. Claims 24-102 are rejected under 35 U.S.C. 112, first paragraph for alleged lack of enablement. The Federal Circuit and its predecessor determined that the utility requirement of 35 U.S.C. § 101 and the how to use requirement of 35 U.S.C. § 112, first paragraph, have the same basis, *i.e.*, the disclosure of a credible utility. *See In re Brana*, 51 F.3d 1560, 1564, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); *see also* M.P.E.P. § 2107(IV); Utility Examination Guidelines at 1098. As discussed above, the specification teaches specific and well-established utilities of the claimed invention, thereby enabling the skilled

artisan to use the claimed polypeptides. Since the specification contains a detailed description of how to use the claimed polypeptides, and the specification describes specific and immediate utilities for the claimed invention, the claimed invention is enabled. Accordingly, it is respectfully requested that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

B. The Examiner further alleges that:

> The skilled artisan would not know what functions or activities polypeptides that are 90-95% identical to the polypeptides disclosed in the specification would retain, or polypeptides that can have from one to 30 amino acid substitutions to those polypeptides, or for polypeptides comprising a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 in which 1 or more amino acid residues are substituted, deleted or added, in any combination, and wherein said polypeptide binds an antibody specific for the polypeptide of SEQ ID NO:2.

Applicants respectfully disagree.

Applicants submit that claims 64 and 76, have been amended to recite the phrase "wherein the polypeptide comprising said first amino acid sequence has immune cell proliferative activity", and claims 40, 100 and 101 have been amended to recite "wherein said isolated polypeptide has immune cell proliferative activity" and to remove part (c) of claim 40. Additionally, claim 102 has been amended to remove subpart (c), remove the antibody binding limitation, and state that the isolated proteins claimed possess immune cell proliferative activity. All of these amendments are supported throughout the specification as filed, for example, at page 96, lines 19-22. Claims 50 and 51 have been amended to recite "wherein said polypeptide inhibits immune cell proliferation". New claim 104 is directed to polypeptides that are at least 90% identical to the soluble extracellular domain of the protein of the instant invention and that inhibit immune cell proliferation. Support for these amendments can be found, for example, in the specification at page 84, lines 29-31. Biological assays including assays to determine the effect of a protein on T cell proliferation are disclosed in the specification, for example, at pages 150-151, Example 14 and at pages 154-156, Example 17. Applicants reserve the right to prosecute the subject matter of the unamended claims in future continuing applications. In view of the above claim amendments, Applicants submit that one of skill in the art *would* know how to make and use the claimed polypeptides. Therefore, Applicants respectfully request that the Examiner

reconsider and withdraw the rejection of claims 24-102 under 35 U.S.C. §112, first paragraph.

C. Claims 40-102 have been rejected by the Examiner under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants respectfully disagree.

The test for the written description requirement is whether one of ordinary skill in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Further, the Federal Circuit recently re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). The court emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification, *rather than whether the specific embodiments had been explicitly described or exemplified.* Indeed, as the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001 (emphasis added).

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one of ordinary skill in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, the Examiner has not met this burden.

Applicants submit that the instant specification clearly teaches N- and C-terminal deletion mutants on, for example, page 40, line 1 through page 49, line 23 of the specification, while variants exhibiting certain % identity are disclosed on page 18, line 21 through page 20, line 1. Additionally, preferred fragments are taught on page 10 of the specification and the specification further teaches that most of these mutations can be made

without affecting the biological activity of the protein (*see* page 39, lines 17-30). Therefore, Applicants have clearly contemplated the many species within the scope of the instant claims.

In addition to the claim amendments described in the previous section, Applicants submit that claims 50 and 51 have been amended and claims 103 and 104 added to capture the extracellular portion of the protein shown to possess inhibitory activity. Applicants feel that the above stated objection has been overcome or obviated by the above amendments and respectfully request that the written description rejection under 35 U.S.C. §112, first paragraph be reconsidered and withdrawn.

III. Conclusion

In view of the foregoing amendments and remarks, Applicants believe that this application is now in condition for allowance.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: September 9, 2002

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Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Moore et al.

Application Serial No.: 09/376,430 Art Unit: 1646

Filed: August 18, 1999 Examiner: O'Hara, E.

For: **Cytokine Receptor Common Gamma Chain Like** Attorney Docket No.: PF466P1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

40. (Twice Amended) An isolated polypeptide having immune cell proliferative activity comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence comprising residues m to 371 of SEQ ID NO:2, where m is an integer in the range of +2 to +370; and

(b) an amino acid sequence comprising residues 1 to n of SEQ ID NO:2, where n is an integer in the range of +2 to +371; ~~and~~ .

~~(c) an amino acid sequence comprising residues m to n of SEQ ID NO:2; where m is an integer in the range of +2 to +370 and n is an integer in the range of +2 to +371, and wherein said amino acid sequence comprises at least seven contiguous amino acid residues of SEQ ID NO:2;~~

50. (Once Amended) An isolated polypeptide comprising at least 30 contiguous amino acid residues of SEQ ID NO:2 wherein said polypeptide inhibits immune cell proliferation.

51. (Once Amended) An isolated polypeptide comprising at least 30 contiguous amino acid residues encoded by the cDNA in ATCC Deposit No. 209691 or 209641 wherein said polypeptide inhibits immune cell proliferation.

64. (Once Amended) An isolated polypeptide comprising a first amino acid sequence 90% or more identical to a second amino acid sequence selected from the group consisting of:

(a) amino acids +1 to +371 of SEQ ID NO:2;

(b) amino acids +2 to +371 of SEQ ID NO:2;

(c) amino acids +23 to +371 of SEQ ID NO:2; and

(d) amino acids +23 to +231 of SEQ ID NO:2,

~~wherein percent identity is calculated using FASTDB with parameters set such that percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acids in the reference amino acid sequence are allowed.~~ ;

wherein the polypeptide comprising said first amino acid sequence has immune cell proliferative activity.

76. (Once Amended) An isolated polypeptide comprising a first amino acid sequence 90% or more identical to a second amino acid sequence selected from the group consisting of:

(a) an amino acid sequence of the full length polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(b) an amino acid sequence of the full length polypeptide, excluding the N-terminal methionine residue, encoded by the cDNA in ATCC Deposit No. 209691 or 209641; and

(c) an amino acid sequence of the mature polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641; ~~and~~

~~(d) an amino acid sequence of the soluble extracellular domain of the polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641~~

~~wherein percent identity is calculated using FASTDB with parameters set such that percentage of identity is calculated over the full length of the reference amino acid sequence and that gaps in homology of up to 5% of the total number of amino acids in the reference amino acid sequence are allowed.~~;

wherein the polypeptide comprising said first amino acid sequence has immune cell proliferative activity.

100. (Once Amended) An isolated polypeptide comprising an amino acid sequence, wherein, except for one to 30 amino acid substitutions, said amino acid sequence is identical to contiguous amino acid residues selected from the group consisting of:

(a) amino acid residues +1 to +371 of SEQ ID NO:2;

(b) amino acids residues +2 to +371 of SEQ ID NO:2;

(c) amino acids residues +23 to +371 of SEQ ID NO:2;

(d) amino acid residues +1 to +231 of SEQ ID NO:2; and

(e) amino acids residues +23 to +231 of SEQ ID NO:2~~.~~;

wherein said isolated polypeptide has immune cell proliferative activity.

101. (Once Amended) An isolated polypeptide comprising an amino acid sequence, wherein, except for one to 30 amino acid substitutions, said amino acid sequence is identical to contiguous amino acid residues selected from the group consisting of:

(a) an amino acid sequence of the full length polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(b) an amino acid sequence of the full length polypeptide, excluding the N-terminal methionine residue, encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(c) an amino acid sequence of the mature polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(d) an amino acid sequence of the extracellular domain of the polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641; and

(e) an amino acid sequence of the soluble extracellular domain of the polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641~~.~~;

wherein said isolated polypeptide has immune cell proliferative activity.

102. (Once Amended) An isolated protein comprising a polypeptide selected from the group consisting of:

(a) a polypeptide consisting of amino acid residues +1 to +371 of SEQ ID NO:2, in which 1 or more amino acid residues are substituted, deleted or added, in any combination and wherein said polypeptide ~~binds an antibody specific for the polypeptide of SEQ ID NO:2;~~ has immune cell proliferative activity; and

(b) a polypeptide consisting of a fragment of SEQ ID NO:2 which fragment has immune cell proliferative activity~~.~~ ~~and in which 1 or more amino acid residues are substituted, deleted, or added, in any combination; and~~

~~(c) a polypeptide consisting of a fragment of SEQ ID NO:2 which fragment has immune cell proliferative activity and in which 1 or more amino acid residues are substituted, deleted or added, in any combination and wherein said polypeptide binds an antibody specific for the polypeptide of SEQ ID NO:2.~~

103. (New) An isolated polypeptide having immune cell growth-inhibitory activity comprising residues 1 to n of SEQ ID NO:2, where n is an integer in the range of +2 to +371, and wherein said polypeptide comprises at least seven contiguous amino acid residues of SEQ ID NO:2.

104. (New) An isolated polypeptide comprising a first amino acid sequence 90% or more identical to a second amino acid sequence of the soluble extracellular domain of the polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641, wherein the polypeptide comprising said first amino acid sequence acts to inhibit immune cell proliferation.